Exhibit G

WARNING LETTER

Lantech Pharmaceuticals Limited

MARCS-CMS 580027 — AUGUST 08, 2019

Delivery Method:

VIA UPS

Product:

Drugs

Recipient:

Mr. V. Prakash Reddy

Managing Director

Lantech Pharmaceuticals Limited

H. No. 7-2-1735 & 1813/5/A1, Flat 101
SBH Building, CZECH Colony, Street No. 2
Sanath Nagar, Hyderabad 500018 Telangana
India

Issuing Office:

Center for Drug Evaluation and Research

10903 New Hampshire Avenue
Silver Spring, MD 20993
United States

Via UPS **Warning Letter** 320-19-34

Return Receipt Requested

August 8, 2019

Mr. V. Prakash Reddy

Managing Director

Lantech Pharmaceuticals Limited

H. No. 7-2-1735 & 1813/5/A1, Flat 101

SBH Building, CZECH Colony, Street No. 2

Sanath Nagar, Hyderabad - 500 018, Telangana

India

Dear Mr. Reddy:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Lantech Pharmaceuticals Limited, FEI 3012390454, at Sy. No. 78, 79, 80, & 145, Chittivalasa, Pydibhimavaram, Ranastalam, Andra Pradesh, from March 6 to 15, 2019.

This warning letter summarizes significant deviations from current good manufacturing practice (CGMP) for active pharmaceutical ingredients (API).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your API are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your April 5, 2019, response in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigators observed specific deviations including, but not limited to, the following.

1. **Failure of your quality unit to ensure that quality-related complaints are investigated and resolved.**

Our inspection found that your firm acts as a contract solvent recovery facility for your customer's valsartan API manufacturing operations; and as contract manufacturer for the API intermediate, lamivudine coupled ester (LVC). In December 2018, your firm was notified by your customer, **(b)(4)**, that **(b)(4)** solvent recovered by your firm contained the potential mutagenic impurity, N-Nitrosodiethylamine (NDEA).
Your firm opened an investigation in response to **(b)(4)** findings as part of their investigation into contaminated valsartan API. However, your investigation was inadequate for the following reasons:

- Your investigation focused on NDEA, although **(b)(4)** notified your firm that they had also identified the potential mutagenic impurity N-Nitrosodimethylamine (NDMA) in samples collected from your equipment used to recover **(b)(4)**.
- The scope of your investigation failed to include non-dedicated storage, receiving, and charging tanks used in your solvent recovery operations. Given that your firm does not maintain logbooks or documentation demonstrating product use or cleaning associated with the use of these tanks, there is a potential for all products manufactured at your facility to contain nitrosamines through mix-ups or cross contamination.
- Your firm manufactures angiotensin II receptor blockers (ARBs) including valsartan, telmisartan, and olmesartan API and intermediates for non-U.S. supply chains. Your firm failed to adequately evaluate the potential of these ARBs to form nitrosamines and identify potential cross contamination risks for drugs manufactured made using non-dedicated equipment and shipped into the U.S. supply chain.

In your response, you stated that you were unaware of specific aspects of your customer's valsartan API manufacturing process which were important for predicting nitrosamine formation in the solvent recovery process. Your response is inadequate because it is your responsibility to understand all the potential risks associated with the drug manufacturing processes conducted at your facility.

We acknowledge that you suspended processing recovered solvents for customers, indicating that additional controls will be put in place should you decide to resume operations in the future. However, your firm has not provided sufficient details or procedures to demonstrate a capability of predicting, controlling, and preventing impurities or cross contamination associated with your solvent recovery processes.

In response to this letter, provide the following:

- A comprehensive, independent assessment of your overall system for investigations of deviations, atypical events, complaints, out-of-specification results, and failures. Your corrective action and preventive action (CAPA) should include but not be limited to improvements in investigation competencies, root cause analysis, written procedures, and quality unit oversight. Also include your process for evaluating CAPA effectiveness.

- An updated nitrosamine investigation to include a detailed risk assessment for all materials produced at your site and the potential to form nitrosamines. The investigation should not be limited to NDMA and NDEA but include a broader evaluation of nitrosamine formation.
- An assessment of all non-dedicated equipment used to manufacture materials for the U.S. supply chain, including API, intermediates, solvents, and starting materials. For all shared equipment, provide details of potential impurities in non-U.S. materials and your controls to prevent cross contamination.
- A list of all customers for whom you have processed recovered solvents in the previous three years. Include a risk assessment for all customer-recovered solvents with emphasis on those solvents which may have originated from high-risk manufacturing operations and pose a safety concern.

2. **Failure to have adequate cleaning procedures to prevent contamination or carry-over of a material that would alter the quality of the API.**

Your firm does not maintain logbooks for product use and cleaning of non-dedicated storage, receiving, and **(b)(4)** solvent recovery tanks. Additionally, during our inspection, solid and liquid material of unknown origin was noted pooling at the bottom of a non-dedicated receiving tank, **(b)(4)**-402. Unknown residue was also observed in the external view glasses, a product contact surface, of non-dedicated receiving tanks **(b)(4)**RT-401, **(b)(4)**RT-402, **(b)(4)**RT-403, and **(b)(4)**RT-410.

In your response, you stated that the tanks will be cleaned **(b)(4)** or after **(b)(4)** batches. Your response is inadequate. No scientific justification was provided for these cleaning frequencies. Additionally, your response did not discuss probable cross contamination or potential mix-up risks associated with these non-dedicated tanks.

Your cleaning validation associated with LVC intermediate production on non-dedicated equipment is also inadequate as you could not provide justification for the swab sample location taken near the **(b)(4)**.

Your response included updates to your cleaning validation procedure. However you failed to commit to revalidating your cleaning procedure for LVC production in accordance with your new procedure.

In response to this letter, provide the following:

- A comprehensive plan to evaluate the adequacy of cleaning procedures, practices, and validation studies for each piece of non-dedicated manufacturing equipment.

- Scientific rationale for your cleaning validation strategy to ensure that the efficacy of your cleaning procedures is adequately assessed.

- A summary of updates to your cleaning validation protocol to better incorporate conditions identified as worst case. This should include but not be limited to evaluating drugs and materials that are of highest toxicity; that are lowest solubility in their cleaning solvents or that have characteristics that make them difficult to clean; and swabbing of various equipment locations that are most difficult to clean.

- A summary of SOP that have been updated to ensure an appropriate program for verification and validation of cleaning procedures for new products, processes, and equipment.

3. **Failure to control and monitor procedures to recover solvents to ensure that they meet appropriate standards before reuse.**

Your firm failed to implement procedures to evaluate and control impurity risks associated with your solvent recovery operations done under contract to API manufacturers. This includes adequate testing to confirm their suitability for manufacturing processes in which they may be used, establishing an impurity profile for solvents to ensure that they meet appropriate standards and maintaining an ongoing program for monitoring process controls to ensure stable manufacturing and prevent unanticipated impurities.

Your firm also failed to implement a procedure for investigating unknown peaks in recovered solvent chromatograms observed during analytical testing. Unknown peaks observed in chromatograms may represent unanticipated impurities and should be thoroughly investigated.

Your firm stated that while you "overlooked" conducting process validation for solvent recovery operations either for customers or internal use, no batch failed release specifications. Your response is inadequate. We remind you that nitrosamines were detected in solvents recovered by your firm; and note that you had not implemented procedures for identifying and investigating unknown peaks in recovered solvent analytical testing.

In response to this letter, provide the following:

- A detailed plan describing how you will implement an ongoing program for monitoring process control to ensure stable manufacturing and prevention of unanticipated impurities during solvent recovery operations.
- A procedure requiring an impurity profile analysis and risk assessment for all solvent recovery operations. The scope of the procedure should include recovered solvents for internal and external use.
- An updated procedure for evaluating unknown peaks in chromatograms.

4. **Failure to exercise sufficient controls over computerized systems to prevent unauthorized access or changes to data and failure to have adequate controls to prevent omission of data.**

Your firm failed to implement adequate controls to ensure the integrity of data generated at your facility. For example, the Senior General Manager of Quality is also the Administrator for chromatographic data system software on your Quality Control laboratory instrumentation. The Administrator has full access privileges to computerized systems, including editing, deleting, modifying data, and audit trails. Additionally, your firm admitted to routinely deleting recovered solvents gas chromatography (GC) data older than three months permanently, without any backup.

In your response, you committed to maintain GC solvent data electronically for six years and to establishing unique user names and assigned access levels. Your response is inadequate as it did not include a comprehensive evaluation of your data integrity controls. Your firm also stated that all the chromatograms are available as hard copies. This is not acceptable. Electronic records from laboratory instrumentation such as GC are dynamic: for example, they can have the scale adjusted to provide additional detail in a region. A printout or a static record does not preserve the dynamic record format that is part of the complete original record.

Data Integrity Remediation

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document *Data Integrity and Compliance With Drug CGMP* for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers-guidance-industry (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers-guidance-industry).

We strongly recommend that you retain a qualified consultant to assist in your remediation. In response to this letter, provide the following:

- A comprehensive investigation into the extent of the inaccuracies in data records and reporting including results of the data review for drugs distributed to the United States. Include a detailed description of the scope and root causes of your data integrity lapses.
- A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.
- A management strategy for your firm that includes the details of your global corrective action and preventive action plan. The detailed corrective action plan should describe how you intend to ensure the reliability and completeness of all data generated by your firm including microbiological and analytical data, manufacturing records, and all data submitted to FDA.

CGMP Consultant Recommended

Based upon the nature of the deviations we identified at your firm, we strongly recommend engaging a consultant qualified to evaluate your operations and to assist your firm in meeting CGMP requirements if your firm intends to resume manufacturing drugs for the U.S. market. We also recommend that the qualified consultant perform a comprehensive audit of your entire operation for CGMP compliance and that the consultant evaluates the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Solvent Recovery Operations Suspended

We acknowledge your commitment to suspend "contract solvent recovery processes" at this facility for the U.S. market. If you plan to resume producing recovered solvents for the U.S. supply chain, notify this office in writing.

Conclusion

The deviations cited in this letter are not intended to be an all-inclusive list of deviations that exist at your facility/in connection with your product(s). You are responsible for investigating and determining the causes of these deviations and for preventing their recurrence or the occurrence of other deviations.

If you are considering an action that is likely to lead to a disruption in the supply of drugs produced at your facility, FDA requests that you contact CDER's Drug Shortages Staff immediately, at drugshortages@fda.hhs.gov, so that FDA can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances or interruptions in your drug manufacture under 21 U.S.C. 356C(b) and allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products.

FDA placed your firm on Import Alert 66-40 on June 27, 2019.

Until you correct all deviations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a drug manufacturer.

Failure to correct these deviations may also result in FDA continuing to refuse admission of articles manufactured at Lantech Pharmaceuticals Limited at Sy. No. 78, 79, 80, & 145, Chittivalasa, Pydibhimavaram, Ranastalam, Andra Pradesh into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Under the same authority, articles may be subject to refusal of admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your deviations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov (mailto:CDER-OC-OMQ-Communications@fda.hhs.gov) or mail your reply to:

Rory K. Geyer
Compliance Officer

U.S. Food and Drug Administration

White Oak Building 51, Room 4235

10903 New Hampshire Avenue

Silver Spring, MD 20993

USA

Please identify your response with FEI 3012390454.

Sincerely,

/S/

Francis Godwin

Director

Office of Manufacturing Quality

Office of Compliance

Center for Drug Evaluation and Research

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